

**In the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

**Claim 1. (currently amended)** An oligonucleotide[[,]]  
comprising:

(a) ~~wherein the third nucleotide from the [[3'-]]end-  
thereof is~~ a 2'-O,4'-C-ethylene nucleotide (ENA) unit which is  
the third nucleotide from the 3'-end of the oligonucleotide,  
wherein the nucleotide at the 3'-end is defined as the first  
nucleotide, and the other nucleotides are natural nucleotides;  
and

(b) ~~wherein the oligonucleotide has~~ a nucleotide  
complementary to the reference nucleotide of a target gene at  
the 3'-end position thereof, and ~~has~~ having nucleotides  
complementary to the nucleotide sequence of the target gene at  
the other positions,

or a salt thereof.

**Claim 2. (currently amended)** An oligonucleotide[[,]]  
comprising:

(a) ~~wherein the third nucleotide from the [[3'-]]end-  
thereof is~~ a 2'-O,4'-C-ethylene nucleotide (ENA) unit which is  
the third nucleotide from the 3'-end of the oligonucleotide,

wherein the nucleotide at the 3'-end is defined as the first nucleotide, and the other nucleotides are natural nucleotides; and

(b) ~~wherein the oligonucleotide has~~ a nucleotide complementary to the mutant nucleotide of a target gene at the 3'-end position thereof, and ~~has~~ having nucleotides complementary to the nucleotide sequence of the target gene at the other positions,  
or a salt thereof.

**Claim 3. (currently amended)** An oligonucleotide[[,]]  
comprising:

(a) ~~wherein a nucleotide at the 3'-end nucleotide thereof~~  
of the oligonucleotide which is a nucleotide complementary to the reference nucleotide of a target gene;

(b) ~~wherein a nucleotide which is~~ the second nucleotide from the 3'-end thereof [[ ( ) ] when of the oligonucleotide,  
wherein the nucleotide at the 3'-end is defined as the first nucleotide[[ ( ) ]], the second nucleotide is a nucleotide that is not complementary to the nucleotide of a reference gene;

(c) ~~wherein the oligonucleotide has~~ nucleotides complementary to the nucleotides of the target gene at other positions; and

(d) ~~wherein a nucleotide which is~~ the third nucleotide from the 3'-end thereof [[ ( ) ] when the nucleotide at-  
the [[3'-]] end is defined as the first nucleotide[[ ( ) ]] of the

oligonucleotide is a 2'-O,4'-C-ethylene nucleotide (ENA) unit,  
and the other nucleotides are natural nucleotides,  
or a salt thereof.

**Claim 4. (currently amended)** An oligonucleotide[[,]]  
comprising:

(a) ~~wherein the [[3'-]]end nucleotide thereof is a~~  
nucleotide at the 3'-end of the oligonucleotide which is a  
nucleotide complementary to the mutant nucleotide of a target  
gene;

(b) ~~wherein~~ a nucleotide which is the second nucleotide  
from the 3'-end ~~thereof~~ of the nucleotide, wherein [[()]]~~when~~  
the nucleotide at the 3'-end is defined as the first  
nucleotide[[()]] , the second nucleotide is a nucleotide that  
is not complementary to the nucleotide of a reference gene;

(c) ~~wherein the oligonucleotide has~~ nucleotides  
complementary to the nucleotides of the target gene at the  
other positions; and

(d) ~~wherein~~ a nucleotide which is the third nucleotide  
from the 3'-end ~~thereof~~ of the oligonucleotide [[()]]~~when the~~  
~~nucleotide at the [[3'-]]end is defined as the first~~  
~~nucleotide[[()]]~~ is a 2'-O,4'-C-ethylene nucleotide (ENA) unit,  
and the other nucleotides are natural nucleotides,  
or a salt thereof.

**Claim 5. (currently amended)** ~~[[An]]~~ The oligonucleotide or a salt thereof according to any one of claims 1 to 4, ~~characterized by having~~ wherein the oligonucleotide has a base length of 18 to 25 bases.

**Claim 6. (canceled)**

**Claim 7. (canceled)**

**Claim 8. (currently amended)** A method for detecting gene polymorphism~~[[,]]~~ comprising ~~the following steps (a) and (b):~~

(a) ~~[[a]] step of~~ performing a PCR with a template nucleic acid of a target gene comprising a genetically polymorphic sequence ~~as a template using~~ ~~[[an]]~~ , said PCR being carried out with a first oligonucleotide which is an oligonucleotide according to any one of claims 1 to ~~[[5]]~~ 4 and ~~[[an]]~~ a second oligonucleotide capable of amplifying a sequence of interest together with said first oligonucleotide in the PCR; and

(b) ~~[[a]] step of~~ determining the presence or absence of gene polymorphism in the nucleic acid based on whether or not a reaction product ~~can be~~ is generated in step (a).

**Claim 9. (currently amended)** A method for determining the nucleotide sequence of a genetically polymorphic sequence[[,]] comprising ~~the following steps (a) and (b):~~

(a) ~~[[a]] step of performing a~~ PCR with a template nucleic acid of a target gene comprising a genetically polymorphic sequence as a template using [[an]] , said PCR being carried out with a first oligonucleotide which is an oligonucleotide according to any one of claims 1 to [[5]] 4 and [[an]] a second oligonucleotide capable of amplifying the sequence of interest together with said first oligonucleotide in the PCR; and

(b) ~~[[a]] step of determining the nucleotide sequence of a genetically polymorphic sequence in the nucleic acid based on whether or not a reaction product can be~~ is generated in step (a).

**Claim 10. (currently amended)** ~~[[A]] The method according to claim 8 [[or 9]], characterized by using [[,]] for detection of the presence or absence of generation of a reaction product wherein the determining of whether or not a reaction product is generated is carried out by at least one or more method selected from the group consisting of electrophoresis, TaqMan PCR [[,]] and [[a]] MALDI-TOF/MS method.~~

**Claim 11. (currently amended)** ~~[[A]]~~ The method according to ~~any one of claims 6 to 10~~ claim 8, ~~characterized in that~~ wherein the gene polymorphism is a single nucleotide polymorphism.

**Claim 12. (currently amended)** A kit for detecting gene polymorphism~~[[,]]~~ ~~which comprises the following (a) to (d)~~ comprising:

(a) ~~[[an]]~~ a first oligonucleotide, wherein the third nucleotide from the 3'-end thereof is a 2'-O,4'-C-ethylene nucleotide (ENA) unit, wherein the nucleotide at the 3'-end is defined as the first nucleotide, the other nucleotides are natural nucleotides, the 3'-end nucleotide thereof is a nucleotide complementary to the reference nucleotide of a target gene, and at the other positions the nucleotides are complementary to the nucleotide sequence of the target gene;

(b) ~~[[an]]~~ a second oligonucleotide capable of amplifying a sequence of interest, together with the first oligonucleotide ~~described~~ set forth in (a) above;

(c) DNA polymerase; and

(d) a PCR buffer.

**Claim 13. (currently amended)** A kit for detecting gene polymorphism~~[[,]]~~ comprising ~~the following (a) to (d):~~

(a) an oligonucleotide, wherein the third nucleotide from the 3'-end thereof is a 2'-O,4'-C-ethylene nucleotide (ENA) unit, wherein the nucleotide at the 3'-end is defined as the first nucleotide, the other nucleotides are natural nucleotides, the 3'-end nucleotide thereof is a nucleotide complementary to the mutant nucleotide of a target gene, and at the other positions the nucleotides are complementary to the nucleotide sequence of the target gene;

(b) a primer capable of amplifying a sequence of interest, together with the oligonucleotide ~~described~~ set forth in (a) above;

(c) DNA polymerase; and

(d) a PCR buffer.

**Claim 14. (currently amended)** A kit for detecting gene polymorphism[[,]] comprising ~~the following (a) to~~[[ (e) ]]:

(a) [[an]] a first oligonucleotide, wherein the third nucleotide from the 3'-end thereof is a 2'-O,4'-C-ethylene nucleotide (ENA) unit, wherein the nucleotide at the 3'-end is defined as the first nucleotide, the other nucleotides are natural nucleotides, the 3'-end nucleotide thereof is a nucleotide complementary to the reference nucleotide of a target gene, and at the other positions the nucleotides are complementary to the nucleotide sequence of [[the]] a target gene;

(b) ~~[[an]]~~ a second oligonucleotide, wherein the third nucleotide from the 3'-end thereof is a 2'-O,4'-C-ethylene nucleotide (ENA) unit, the other nucleotides are natural nucleotides, the 3'-end nucleotide thereof is a nucleotide complementary to the mutant nucleotide of a target gene, and at the other positions the nucleotides are complementary to the nucleotide sequence of the target gene;

(c) ~~[[an]]~~ a third oligonucleotide capable of amplifying a sequence of interest, together with the first oligonucleotide ~~described~~ set forth in (a) above or the second oligonucleotide set forth in (b) above;

(d) DNA polymerase; and

(e) a PCR buffer.

**Claim 15. (currently amended)** A kit for detecting gene polymorphism~~[[,]]~~ comprising ~~the following (a) to (d):~~

(a) ~~[[an]]~~ a first oligonucleotide~~[[,]]~~ having the following characteristics (i) to (iv):

(i) ~~wherein~~ the 3'-end nucleotide ~~thereof~~ of the first oligonucleotide is a nucleotide complementary to the reference nucleotide of a target gene;

(ii) the second nucleotide from the 3'-end ~~thereof~~ [[()]]when-~~of~~ the oligonucleotide, wherein the nucleotide at the 3'-end is defined as the first nucleotide~~[[()]]~~ , the second nucleotide is a nucleotide that is not complementary to the nucleotide of a reference gene;



(iii) ~~wherein~~ the first oligonucleotide has nucleotides complementary to the nucleotides of the target gene at the other positions; and

(iv) ~~wherein~~ the third nucleotide from the 3'-end ~~thereof~~ ~~[[~~(~~)]~~]]~~ ~~when the nucleotide at the~~ ~~[[3'-]]~~ ~~end is defined as the~~ ~~first nucleotide~~ ~~[[~~(~~)]~~]]~~ of the first oligonucleotide is a 2'-O,4'-C-ethylene nucleotide (ENA) unit, and the other nucleotides are natural nucleotides,  
or a salt thereof;~~~~

(b) ~~[[an]]~~ a second oligonucleotide capable of amplifying a sequence interest, together with the first oligonucleotide ~~described~~ set forth in (a) above;

(c) DNA polymerase; and

(d) a PCR buffer.

**Claim 16. (currently amended)** A kit for detecting gene polymorphism~~[[,]]~~ comprising ~~the following (a) to (d):~~

(a) ~~[[an]]~~ a first oligonucleotide~~[[,]]~~ having the following characteristics (i) to (iv):

(i) ~~wherein~~ the 3'-end nucleotide ~~thereof~~ of the first oligonucleotide is a nucleotide complementary to the mutant nucleotide of a target gene;

(ii) ~~wherein~~ the second nucleotide from the 3'-end ~~thereof~~ ~~(when~~ of the first oligonucleotide, wherein the nucleotide at the 3'-end is defined as the first nucleotide

[[ ]], the second nucleotide is a nucleotide that is not complementary to the nucleotide of a reference gene;

(iii) ~~wherein~~ the first oligonucleotide has nucleotides complementary to the nucleotides of the target gene at the other positions; and

(iv) ~~wherein~~ the third nucleotide from the 3'-end thereof ~~[[ ]] when the nucleotide at the [[3'-]] end is defined as the first nucleotide~~ is a 2'-O,4'-C-ethylene nucleotide (ENA) unit, and the other nucleotides are natural nucleotides;

or a salt thereof;

(b) ~~[[an]]~~ a second oligonucleotide capable of amplifying a sequence of interest, together with the first oligonucleotide ~~described~~ set forth in (a) above;

(c) DNA polymerase; and

(d) a PCR buffer.

**Claim 17. (currently amended)** A kit for detecting gene polymorphism[[,]] comprising ~~the following (a) to~~ ~~[[ (e) ]]~~:

(a) ~~[[an]]~~ a first oligonucleotide having the following characteristics (i) to (iv):

(i) ~~wherein~~ the 3'-end nucleotide ~~thereof~~ of the first oligonucleotide is a nucleotide complementary to the reference nucleotide of a target gene;

(ii) ~~wherein~~ the second nucleotide from the 3'-end ~~thereof~~ [[()]]when of the first oligonucleotide, wherein the nucleotide at the 3'-end is defined as the first nucleotide~~[[()]]~~ , the second nucleotide is a nucleotide that is not complementary to the nucleotide of a reference gene;

(iii) ~~wherein~~ the first oligonucleotide has nucleotides complementary to the nucleotides of the target gene at the other positions; and

(iv) ~~wherein~~ the third nucleotide from the 3'-end thereof ~~[[()]]when the nucleotide at the [[3'-]] end is defined as the first nucleotide[[()]]~~ is a 2'-O,4'-C-ethylene nucleotide (ENA) unit, and the other nucleotides are natural nucleotides, or a salt thereof;

(b) [[an]] a second oligonucleotide[[,,]] having the following characteristics (i) to (iv):

(i) ~~wherein~~ the 3'-end nucleotide ~~thereof~~ of the second oligonucleotide is a nucleotide complementary to the mutant nucleotide of a target gene;

(ii) ~~wherein~~ the second nucleotide from the 3'-end ~~thereof~~ [[()]]when of the second oligonucleotide, wherein the

nucleotide at the 3'-end is defined as the first nucleotide~~[[ ]]~~ , the second nucleotide is a nucleotide that is not complementary to the nucleotide of a reference gene;

(iii) ~~wherein~~ the second oligonucleotide has nucleotides complementary to the nucleotides of the target gene at the other positions; and

(iv) ~~wherein~~ the third nucleotide from the 3'-end thereof ~~[[ ]] when the nucleotide at the [[3'-]] end is defined as the first nucleotide[[ ]]~~ is a 2'-O,4'-C-ethylene nucleotide (ENA) unit, and the other nucleotides are natural nucleotides, or a salt thereof;

(c) ~~[[an]]~~ a third oligonucleotide capable of amplifying a sequence of interest, together with the first oligonucleotide ~~described~~ set forth in (a) above or the second oligonucleotide set forth in (b) above;

(d) DNA polymerase; and

(e) a PCR buffer.

**Claim 18. (currently amended)** ~~[[A]]~~ The kit for detecting gene polymorphism according to ~~any one of claims~~ claim 12 ~~[[to 17]]~~, ~~characterized in that an~~ wherein the first oligonucleotide~~[[ , ]]~~ and ~~[[an]]~~ the second oligonucleotide ~~capable of amplifying a sequence of interest together with~~

~~said oligonucleotide~~[[,]] each have a base length of 18 to 25 bases.

**Claim 19. (currently amended)** [[A]] The kit according to any one of claims 12 to 18, ~~characterized in that~~ wherein the gene polymorphism is a single nucleotide polymorphism.

**Claim 20. (new)** The oligonucleotide according to claim 1, wherein the target gene is a drug metabolizing gene.

**Claim 21. (new)** The oligonucleotide according to claim 20, wherein the drug metabolizing gene is selected from the group consisting of cytochrome P4501A2, cytochrome P4502A6, cytochrome P4502C9, cytochrome P4502C19, cytochrome P4502D6 and cytochrome P4502E1.

**Claim 22. (new)** The oligonucleotide according to claim 1, wherein the target gene is selected from the group consisting of thiopurine methyltransferase, N-acetyltransferase, UDP-glucuronosyltransferase and glutathione S-transferase.

**Claim 23. (new)** The oligonucleotide according to claim 1, wherein the target gene is a disease-associated gene.

**Claim 24. (new)** The oligonucleotide according to claim 1, wherein the target gene is selected from the group consisting of a causative gene of ulcerative colitis, a causative gene of arthritis rheumatoides, a causative gene of Alzheimer's disease, a causative gene of schizophrenia, a causative gene of manic-depressive psychosis, a causative gene of albuminuria, a causative gene of myocardial infarction and a causative gene of adiposis.

**Claim 25. (new)** The oligonucleotide according to claim 1, wherein the target gene is selected from the group consisting of HLA, TCR $\alpha$ , APOE4, a dopamine D3 receptor, tryptophan hydroxylase, an angiotensin precursor, a blood coagulation factor VII, leptin and human prothrombin.

**Claim 26. (new)** The oligonucleotide according to claim 2, wherein the target gene is a drug metabolizing gene.

**Claim 27. (new)** The oligonucleotide according to claim 26, wherein the drug metabolizing gene is selected from the

group consisting of cytochrome P4501A2, cytochrome P4502A6, cytochrome P4502C9, cytochrome P4502C19, cytochrome P4502D6 and cytochrome P4502E1.

**Claim 28. (new)** The oligonucleotide according to claim 2, wherein the target gene is selected from the group consisting of thiopurine methyltransferase, N-acetyltransferase, UDP-glucuronosyltransferase and glutathione S-transferase.

**Claim 29. (new)** The oligonucleotide according to claim 2, wherein the target gene is a disease-associated gene.

**Claim 30. (new)** The oligonucleotide according to claim 2, wherein the target gene is selected from the group consisting of a causative gene of ulcerative colitis, a causative gene of arthritis rheumatoides, a causative gene of Alzheimer's disease, a causative gene of schizophrenia, a causative gene of manic-depressive psychosis, a causative gene of albuminuria, a causative gene of myocardial infarction and a causative gene of adiposis.

**Claim 31. (new)** The oligonucleotide according to claim 2, wherein the target gene is selected from the group consisting of HLA, TCR $\alpha$ , APOE4, a dopamine D3 receptor, tryptophan hydroxylase, an angiotensin precursor, a blood coagulation factor VII, leptin and human prothrombin.

**Claim 32. (new)** The oligonucleotide according to claim 3, wherein the target gene is a drug metabolizing gene.

**Claim 33. (new)** The oligonucleotide according to claim 32, wherein the drug metabolizing gene is selected from the group consisting of cytochrome P4501A2, cytochrome P4502A6, cytochrome P4502C9, cytochrome P4502C19, cytochrome P4502D6 and cytochrome P4502E1.

**Claim 34. (new)** The oligonucleotide according to claim 3, wherein the target gene is selected from the group consisting of thiopurine methyltransferase, N-acetyltransferase, UDP-glucuronosyltransferase and glutathione S-transferase.

**Claim 35. (new)** The oligonucleotide according to claim 3, wherein the target gene is a disease-associated gene.



**Claim 36. (new)** The oligonucleotide according to claim 3, wherein the target gene is selected from the group consisting of ulcerative colitis, a causative gene of arthritis rheumatoides, a causative gene of Alzheimer's disease, a causative gene of schizophrenia, a causative gene of manic-depressive psychosis, a causative gene of albuminuria, a causative gene of myocardial infarction and a causative gene of adiposis.

**Claim 37. (new)** The oligonucleotide according to claim 3, wherein the target gene is selected from the group consisting of HLA, TCR $\alpha$ , APOE4, a dopamine D3 receptor, tryptophan hydroxylase, an angiotensin precursor, a blood coagulation factor VII, leptin and human prothrombin.

**Claim 38. (new)** The oligonucleotide according to claim 4, wherein the target gene is a drug metabolizing gene.

**Claim 39. (new)** The oligonucleotide according to claim 37, wherein the drug metabolizing gene is selected from the group consisting of cytochrome P4501A2, cytochrome P4502A6,

cytochrome P4502C9, cytochrome P4502C19, ccytochrome P4502D6 and cytochrome P4502E1.

**Claim 40. (new)** The oligonucleotide according to claim 4, wherein the target gene is selected from the group consisting of thiopurine, methyltransferase, N-acetyltransferase, UDP-glucuronosyltransferase and glutathione S-transferase.

**Claim 41. (new)** The oligonucleotide according to claim 4, wherein the target gene is a disease-associated gene.

**Claim 42. (new)** The oligonucleotide according to claim 4, wherein the target gene is selected from the group consisting of a causative gene of ulcerative colitis, a causative gene of arthritis rheumatoides, a causative gene of Alzheimer's disease, a causative gene of schizophrenia, a causative gene of manic-depressive psychosis, a causative gene of albuminuria, a causative gene of myocardial infarction and a causative gene of adiposis.

**Claim 43. (new)** The oligonucleotide according to claim 4, wherein the target gene is selected from the group

consisting of HLA, TCR $\alpha$ , APOE4, a dopamine D3 receptor, tryptophan hydroxylase, an angiotensin precursor, a blood coagulation factor VII, leptin and human prothrombin.

**Claim 44. (new)** The method according to claim 9, wherein the determining of whether or not a reaction product is generated is carried out by at least one method selected from the group consisting of electrophoresis, TaqMan PCR and MALDI-TOF/MS.

**Claim 45. (new)** The method according to claim 10, wherein the gene polymorphism is a single nucleotide polymorphism.

**Claim 46. (new)** The method according to claim 8, wherein the first oligonucleotide has a base length of 18 to 25 bases.

**Claim 47. (new)** The method according to claim 9, wherein the first oligonucleotide has a base length of 18 to 25 bases.

**Claim 48. (new)** The method according to claim 10, wherein the first oligonucleotide has a base length of 18 to 25 bases.

**Claim 49. (new)** The method according to claim 11, wherein the first oligonucleotide has a base length of 18 to 25 bases.

**Claim 50. (new)** The method according to claim 44, wherein the first oligonucleotide has a base length of 18 to 25 bases.

**Claim 51. (new)** The method according to claim 45, wherein the first oligonucleotide has a base length of 18 to 25 bases.

**Claim 52. (new)** The kit for detecting gene polymorphism according to claim 13, wherein the oligonucleotide has a base length of 18 to 25 bases.

**Claim 53. (new)** The kit for detecting gene polymorphism according to claim 14, wherein the first oligonucleotide, the second oligonucleotide and the third oligonucleotide each have a base length of 18 to 25 bases.

**Claim 54. (new)** The kit for detecting gene polymorphism according to any one of claims 15, 16 or 17, wherein the first oligonucleotide and the second oligonucleotide each have a base length of 18 to 25 bases.